

The Opioid Epidemic:

How Innovative Approaches to Drug Packaging Can Save Lives



It's no secret that the current opioid epidemic is a major **U.S. public health crisis.**


As Scott Gottlieb, M.D., Commissioner of the U.S. Food and Drug Administration (FDA), said recently, the epidemic has reached “tragic proportions.”¹ The U.S. Department of Health and Human Services (HHS) declared the opioid crisis a “public health emergency” in 2017.²

The facts and figures associated with the epidemic are staggering. It has been estimated that in 2017 alone, 11.4 million people in the U.S. misused opioids.³

Federal and state agencies, along with many other types of healthcare organizations, are working to combat the crisis. For example, HHS has initiated a variety of prevention and treatment programs, including research initiatives focused on addiction and pain and projects focused on updating clinical guidelines, increasing access to services, promoting the use of overdose-reversing drugs and promoting safe storage and take-back initiatives. Among these developments are anticipated changes in pharmaceutical product packaging.

“At WestRock, we believe packaging can make a meaningful impact on combating the opioid crisis,” says Dave Dwyer, vice president of Global Marketing, Adherence. “We’ve spent years studying how innovative and informed packaging designs can help change the way patients appropriately initiate, take as prescribed and discontinue their medication. We’ve invested in rigorous, peer-reviewed, published research on how well-designed packaging can help—and that work is continuing.”





"WestRock has developed opioid packaging prototypes that are designed to deliver a broad array of benefits tailored specifically to the challenges posed by this class of drugs."

Dave Dwyer, WestRock's vice president of Global Marketing, Adherence

"WestRock has developed more than 100 adherence package designs that have passed F=1 child-resistant/senior friendly (CR/SF) testing, with more than 50 commercial applications serving the branded pharmaceutical market across multiple therapeutic categories. This scientific evaluation validates the positive adherence, persistence and safety benefits these WestRock proprietary adherence packaging designs provide for patients," Dwyer states.⁴

"Based upon insights gained from our years of experience in the adherence market, WestRock has developed opioid packaging prototypes that are designed to deliver a broad array of benefits tailored specifically to the challenges posed by this class of drugs. We believe opioid manufacturers can meaningfully address the crisis by changing their product packaging from bottles to validated adherence packaging designs," he explains.

Beginning in 2014, through a series of public workshops and notices, the FDA has explored packaging innovation (including calendared blister packaging with and

without electronic systems for monitoring, assessing and improving adherence to medication regimen) and has considered the role of packaging, storage and disposal options in addressing the opioid epidemic. "From the start, due to its research experience, WestRock has been part of those working groups⁵ at the FDA. As a result of these engagements, the FDA has indicated it intends to require changes in the way opioids are packaged across the class, and WestRock has been working with the Agency and with state-based organizations to explore validated options," says Elizabeth Whalley Buono⁶, RN, MBA, JD. In fact, the Opioid Crisis Response Act of 2018 (S. 2680), which was signed into law in October 2018⁷, contains language that clarifies the FDA's authority to do just that.

"As a result of the FDA's regulatory action, brand managers and others in the pharmaceutical industry now have an opportunity to learn about the results of these FDA engagements and take a leading role in customizing packaging initiatives that can help enhance opioid safety," she says.

A photograph of a person from behind, walking down a brightly lit hospital hallway. The person is wearing a grey t-shirt and dark pants. Their left leg is in a white cast and they are using two blue and silver crutches to support themselves. The hallway has orange walls and a polished floor.

The Root of the Opioid Crisis: Pain Management

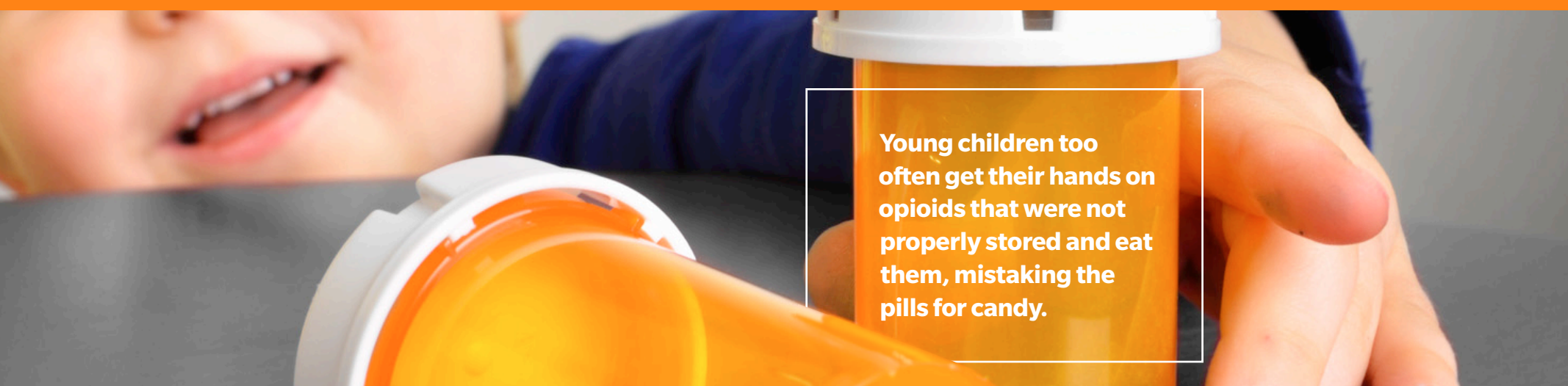
To understand how packaging innovations can help curb opioid misuse, it's important to first understand how people typically get into trouble with prescription opioids.

Legally prescribed opioid medications play an important role in pain management for many people, especially those with cancer pain and other severe chronic pain conditions. Many patients take opioids exactly as they are prescribed with good results.

But as we've seen in recent years, opioids are commonly misused in both intentional and unintentional ways, by both professionals and patients, and this misuse is at the root of the current crisis.

Opioids are prescribed for routine medical conditions.⁸ Opioids are often prescribed for relatively minor medical issues that could possibly be addressed with other treatments. For example, many patients undergoing uncomplicated tooth extractions are prescribed a strong opioid pain reliever when a non-opioid pain medication would suffice.

Opioids are prescribed in excessive amounts.⁹ Currently, that same tooth-extraction patient is likely to be prescribed a 30-day supply of an opioid, when, for example, a three-day supply would be more appropriate.



Young children too often get their hands on opioids that were not properly stored and eat them, mistaking the pills for candy.

Opioids are not stored securely.¹⁰ Typically, patients do not store medications in locked cabinets at home to prevent diversion, the transfer of prescription medications to a non-prescribed individual, nor do they place medications in locations up and away from children and other family members as recommended by the CDC.¹¹

Opioids are not disposed of properly. Instead of disposing unused medications as recommended by the FDA, many people keep unused opioids on hand, “just in case” they are needed in the future.¹²

These practices and others all provide the opportunity for inappropriate access to opioids and often can lead to misuse of those readily available pills.

Unintentional misuse of opioids can also be the result of medication non-adherence. Many patients misunderstand their prescription regimen instructions or fail to track their pill consumption carefully.¹³ These factors can result in patients mistakenly taking more medication than prescribed, which can lead to addiction.

Intentional misuse of opioids is also a factor. When taking opioids for a prescribed use, patients may find they like the feeling they get from them, disregarding or not knowing about the dangers of addiction.

Purely accidental exposures are also a problem. Young children too often get their hands on opioids that were not properly stored and eat them, mistaking the pills for candy.

Lastly, diversion is a major issue within households and workplaces. Family members and visitors who have not been prescribed the medication may find accessible drug vials tempting. “No one will notice if I swipe a few pills,” they think. Healthcare workers, too, will sometimes divert workplace opioids for their personal use.

All in all, the vast majority of prescription pills that are misused originate from medical prescriptions. And the majority of people who misuse them—53 percent—obtain them from a friend or relative, usually for free and often without the other person’s knowledge.¹⁴ Fewer than six percent of those who misuse prescription pills obtain them from a drug dealer or stranger. Based upon what we’ve learned over the last few years, the all-too-common scenarios noted above can lead to addiction, as well as fatal overdoses.

Innovative Packaging Design Can Make a Difference

WestRock's scientifically validated¹⁶ packaging prototypes offer real-world potential for helping to combat these issues. These prototypes can help all stakeholders—packagers, brand managers, pharmacies, regulatory agencies and others—to understand how packaging can make a difference.

Specifically, WestRock's proprietary calendared blister package (Figure 1) incorporates an array of features that can help increase patient medication adherence and persistence, thereby potentially decreasing both unintentional and intentional misuse of opioids and potentially reducing the incidence of undetected diversion of pills by household visitors and others.

The inner calendared blister card feature helps patients track and take their medication correctly, improving adherence and appropriate discontinuation, thus potentially helping patients more effectively manage pain while potentially minimizing the risk of complications such as addiction and overdose. In the blister card, each pill is contained in an individual, numbered cavity. Patients are encouraged to enter the prescription start date on the back side of the card and then to take the pills in numerical order, per their prescription. This makes it easier for patients to see when they are due to take a pill, as well as when they are not due, potentially minimizing the risk of accidental misuse.

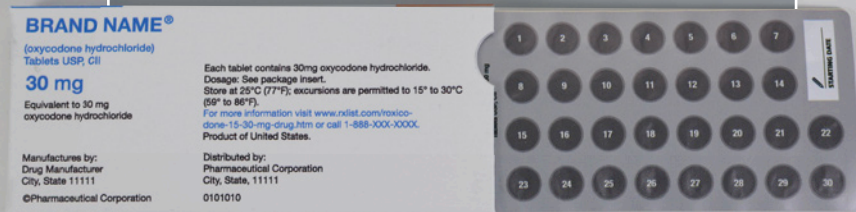


Figure 1
Dosepak® Express

Dosepak® Express

Blistercard: This calendared medication blistercard will help patients track and take their medication correctly:

- By writing in their start date, patients can utilize numbered pill cavities to track their medication use and improve adherence.
- Tamper evident blister design helps reduce erroneous complaints of pharmacy short fills
- Clear blister cavity design will help patients immediately recognize when pills have "gone missing" in the home.
- Blister layout may reduce likelihood of diversion by family members - further evaluation required.



The card contains the exact number of pills prescribed, making it clear to the patient how long they should be taking the prescription. The package can accommodate a smaller number of pills than the ubiquitous 30-day supply. This makes it ideal for dispensing the Centers for Disease Control's three-, five-, and seven-day opioid regimens for short-term use, eliminating "leftover" pills that end up sitting on a shelf.

The calendared blister card can help prevent intentional misuse and diversion by other members of the household as well. A patient who is taking pills by the number is more likely to immediately notice when pills have gone missing, as compared to loose pills dispensed in a vial or bottle. Evidence shows that the detection of missing pills from vials is more difficult than the detection of missing pills from, for example, a blister package.¹⁷ This feature also reduces the likelihood of erroneous complaints that the pharmacy did not dispense to the patient all of the pills prescribed.

The blister card and outer package component are specifically designed to help reduce accidental overdoses. We know that pill vials often are not correctly closed and can easily be spilled. We also know that any patient can request that their medication be dispensed in non-child-resistant vials at the pharmacy. WestRock's outer tear-resistant package component features proprietary "push-and-pull" child-resistant technology that is integral to the package, a feature that is also senior-friendly. Listed as a "recognized child-resistant feature" in the ASTM D-3475, the technology has been dispensed for more than 1 billion prescriptions with no reported CR failures.¹⁸



To access pills in WestRock's produced package, the patient simply presses down on a button while simultaneously pulling out the blister card, potentially reducing the chance of spillage. After the dose is removed, the blister card is reinserted to reliably re-engage the child-resistant feature.

Importantly, unlike a bottle or vial, the package design accommodates readable and critical patient education information. The package is designed with ample flat "billboard" space that can be printed with important labeling, prescribing information, educational content, health warnings, emergency contact information, disposal instructions, and links to support resources, such as the federal Substance Abuse and Mental Health Services (SAMHSA) substance abuse treatment hotline. Additionally, the space can accommodate QR and barcodes that link patients to additional resources and information. And because the outer package stays with the drug throughout the product's life cycle, patients will see this information every time they hold the package.

"It's important that product and patient information are presented in a readable manner, and that it will not be thrown away as traditional paper inserts customarily

are," says Whalley Buono. "Through WestRock's packaging, the patient is engaged with critical information every single time they take a medication."

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For a more high-tech application, the package can be fitted with advanced electronic monitoring technologies, such as sensors that record when a pill is removed from the blister card. Such monitoring systems can potentially help prescribers and others to integrate daily adherence information into an electronic health record, as well as to raise alarms when a patient obtains opioid prescriptions from several providers within a short period of time.

A photograph of two male scientists in a laboratory setting. They are both wearing white lab coats and safety glasses. The scientist in the foreground is pointing at a tablet held by the second scientist. They appear to be engaged in a collaborative discussion. The background is slightly blurred, showing laboratory equipment and a bright, clean environment.

Scientifically Validated Design Concepts

The features incorporated into WestRock's calendared blister package design have been validated in peer-reviewed scientific studies published in noteworthy journals. Predicate package designs have been proven to improve adherence and persistence and in a recent first-of-its-kind, prospectively designed packaging study, patients found the packages to be easy to use.¹⁹

WestRock recently funded the first and only prospective clinical research trial evaluating the effect of calendared blister packaging on medication adherence and health outcomes.²⁰ That study, conducted in the Department of Veterans Affairs (VA) healthcare system, compared cholesterol medication refill rates of patients who received their medication in a calendared blister package to those who received standard medication packaging (loose pills in a vial). Over 12 months, patients who received the blister package showed a 7.6 percent increase in refill rates.

"That translates to an extra month of access to medication," says Hayden B. Bosworth, lead author of the study and Associate Director of the Center for Health Services Research in Primary Care, Principal Investigator for the VA Office of Academic Affairs PhD Post-Doctoral training grant. "It would be hard for anyone to argue that an extra month of prescription use of a statin is not clinically meaningful. And patients found the packaging easy to use."

"Looking at adherence studies," Bosworth continues, "this is probably the only intervention I can think of that potentially is cost effective. It doesn't cost very much. This is not going to solve the whole opioid situation, but it is part of the toolbox."

Currently, WestRock is also working with the state of Connecticut to implement a study that will evaluate the impact of calendared blister packaging specifically on the use of opioid medications for acute pain after dental or orthopedic surgery.

"The WestRock calendared blister package prototype addresses many of the issues that the FDA has raised in discussions on the potential of packaging standards to address the opioid epidemic by significantly reducing misuse, including improving adherence, providing educational information, making lower-count dispensing easier, preventing diversion and improving trackability," says Whalley Buono.

"We believe that widespread use of such a package could help move the needle on addressing the opioid crisis."

Elizabeth Whalley Buono, RN, MBA, JD





About WestRock

WestRock (NYSE: WRK) partners with our customers to provide differentiated paper and packaging solutions that help them win in the marketplace. WestRock's 50,000 team members support customers around the world from more than 320 operating and business locations spanning North America, South America, Europe, Asia and Australia. Learn more at [westrock.com](https://www.westrock.com).

For more information on WestRock's healthcare packaging solutions, visit:

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Sample of WestRock Dosepak® packaging highlighting instructional label.



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